



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Nicolaides et al.

Confirmation No.: 6480

Serial No.:

09/853,646

Group Art Unit: 1632

Filing Date: May 14, 2001

Examiner:

R.R. Shukla

For: A METHOD FOR GENERATING HYPERMUTABLE ORGANISMS

RECEIVED

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

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TECH CENTER 1600/2900

Declaration under 37 CFR 1.131

I, Nicholas C. Nicolaides, hereby state the following:

- I-earned my doctorate in Genetics at Thomas Jefferson University in Philadelphia, Pennsylvania.
- I am a founder of Morphotek Inc., and serve as President, Chief Executive Officer and Chief Science Officer.
- I am an inventor of the above-referenced patent application and am thoroughly familiar with the field of molecular biology, and in particular, mismatch repair.
- 4. In accordance with the teachings of our specification, we have generated a dominant negative mutant form of a plant PMS2 from Arabidopsis thaliana.
- The following describes the experiments for expression of an Arabidopsis thaliana PMS2 truncation mutant in bacteria:

An Arabidopsis thaliana dominant negative MMR gene mutant was created by generating a construct with similar domains to that of the human dominant negative PMS2 gene (referred to as hPMS2-134). To generate this vector, the A. thaliana PMS2 (ATPMS2) and human PMS2 (hPMS2) cDNA sequences were aligned and the conserved domain was isolated. Figure 1 shows a sequence alignment between the human and A. thaliana PMS2-134 amino acid sequences wherein a 51% identity is found between the